REMARKS

I. Status of the Claims

With this amendment, claims 1-77 are pending in the present application. Claims 1-9 and 24-77 are withdrawn. Claims 10-23 are under examination.

II. Rejection under 35 U.S.C. 103(a)

Claims 10-17 are rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Guo *et* al. (1994), in view of Moviglia (1996). Applicants respectfully traverse the rejection and its supporting remarks.

As noted by the Examiner, Guo *et al.* only teach that tumor/B cell hybrids "***may*** provide a useful strategy for cancer immunotherapy." Office Action dated 6/12/07, page 3. Further, the Examiner cites to Dr. Moviglia's publication in 1996 regarding use of tumor/B cell hybrids to treat humans. Unfortunately, the method taught in Dr. Moviglia's publication did not result in an effective therapeutic. As indicated in paragraph [0003] of the specification, use of tumor/APC hybrids, whether using B-cells or dendritic cells, does not provide sufficient immune response in cancer patients, which the inventor of the presently claimed invention, Dr. Moviglia, attributes to suppression of the immune recognition by the tumor cells. It was that very insight that lead Dr. Moviglia to create the novel therapy disclosed in the specification, specifically, loading dendritic cells outside of the body with tumor antigens using tumor/B-cell hybrids to circumvent the tolerance. Thus, since tumor/B-cell hybrids have not been proven to be an effective therapeutic such that the author of one of the papers cited in the obviousness rejection was forced to move on to a modified therapy regime, one of skill in the art would not be motivated to use Guo *et al* (1994) or Moviglia (1996) as a starting point to make the modifications asserted by the Examiner to be obvious.

Further, the Examiner has created a reason for modifying Guo *et al* (1994) and Moviglia (1996) without citing to any source for the asserted reason for modifying. The Examiner has stated that, "The ordinary artisan would want to have more activated CD8+ cells available for the killing of tumor cells in the host, especially when the host does not have sufficient competent CD8+ cells." The Examiner has not cited to any teaching that a patient lacks sufficient competent CD8+ cells. Neither Guo *et al.* (1994) nor Moviglia (1996) cite to a lack of CD8+ cells that would lead one of skill in the art to believe that more are needed. Given that any procedure such as that claimed performed *ex vivo* carries with it a risk of introducing infection into a patient, one of skill in the art would look to other methods of increasing CD8+ response (assuming such lack were even recognized in the art) that minimize *ex vivo* manipulations. As discussed below, dendritic cells are perceived in the art to be the best at antigen presentation and priming CD4+ and CD8+ responses. Thus, one of skill in the art would naturally choose to try dendritic cells as a better alternative, which is what has happened in the art as described below.

Even if one of skill in the art were to be motivated to modify a tumor/antigen presenting cell hybrid system, it would be the tumor/dendritic cell hybrid system. As indicated in the specification, most, if not all, in the field of immunology believe that dendritic cells are much better at antigen presentation at least in the context of cancer immuno-therapy. Compare the two relatively early publications by Guo *et al.* (1994) and Moviglia (1996) with the eight later publications where persons of ordinary skill in the art pursued: Tanaka *et al.* 2000, Gong *et al.* 2002, Homma *et al.* 2001, Wang *et al.* 1998, Celluzzi *et al.* 1998, Gong *et al.* (I) 2000, Gong *et al.* (III) 2000, Li *et al.* 2001, and Gong *et al.* 1997. Gong *et al.* (2002) state in their introduction (p. 2512):

> Dendritic cells (DCs) are potent antigen presenting cells (APC) that initiate primary immune responses. DCs are distinguished from B lymphocytes and macrophages by their abundant expression of major histocompatibility complex (MHC) class I, class II, costimulatory molecules, and adhesion molecules which provide secondary signals for the stimulation of naïve T-cell populations.

Thus, Gong *et al.* (2002) teach that DCs are superior to B cells.

Celluzi *et al.* (1998) teach that, "Dendritic cells (DCs) are the ***most potent APCs identified*** thus far, and adoptive transfer of Ag-loaded DCs can induce effective CTL-dependent antitumor immunity." Pg 3081, right col., last paragraph (citations omitted).

Wang *et al.* (1998) similarly teach that, "In the past several years, dendritic cells (DCs) have been identified as ***the most effective APC***." Page 5516, right col., first full paragraph.

Thus, all of these would lead one of skill in the art to use tumor/dendritic cell hybrids as they teach away from using any other antigen presenting cells. In fact, even the inventor, Dr. Moviglia has moved away from using the tumor/B-cell hybrids as the antigen presenting cell. Dr. Moviglia himself switched to using the tumor/B-cell hybrid to load DCs *ex vivo*, which are then introduced into the patient as the antigen presenting cells.

In addition, one of skill in the art would not have a reasonable expectation of success. As is shown by the numerous papers on tumor/DC hybrids cited above, a significant amount of time and effort is being devoted to working on tumor/DC hybrids to generate a useable and efficacious therapeutic system. If it were so simple and predictable for one of skill in the art to combine existing teachings to come up with a workable system, tumor/DC hybrids would be used today rather than being experimental therapeutics undergoing a significant degree of modification and adaptation. Thus, one of skill in the art, until the teaching of this specification which demonstrates the efficacy of CD8+ cells expanded *ex vivo* using tumor/B-cell hybrids, would not have a reasonable expectation of success.

Thus, the presently claimed invention is not obvious over Guo *et al.* (1994) in light of Moviglia (1996) since there is no reason that one of skill in the art would modify what ended up being a failed system. Further, all of the art since has taught use of dendritic cells, actually teaching away from use of B-cells as antigen presenting cells. Finally, one of skill in the art would not have a reasonable expectation of success, especially in light of the failure of tumor/B-cell hybrids to produce an efficacious therapeutic. To date, every one of skill in the art has been motivated to switch to using = dendritic cells to solve the problem of lack of efficacy of tumor/B-cell hybrids.

Applicants therefore respectfully request the withdrawal of the rejection of claims 18-23 under 35 U.S.C. § 103(a).

III. Rejection under 35 U.S.C. 103(a)

Claims 18-23 are rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Guo *et* al. (1994), in view of Moviglia (1996) and Gong *et al.* (WO 01/59073). Applicants respectfully traverse the rejection and its supporting remarks.

For the reasons discussed above, one of skill in the art would not be motivated to make the modifications asserted by the Examiner as the art teaches away from use of B-cell as antigen presenting cells.

Gong *et al.* fail to remedy this. The Examiner cites to Gong *et al.* for support for exposure of CD8+ cells with "fused cell" to expand the CD8+ cells *ex vivo*. However, the specification of Gong *et al.* starting on page 9, line 30 and ending on page 13, line 9, discusses the fused cells and all of the discussion relates to fusion of dendritic cells as APCs with other cells. Thus, Gong *et al.* further re-enforces that one of skill in the art would not be motivated to use B-cells. Gong *et al.* set out to solve the problem of expanding CD8+ cells *ex vivo* and chose to use dendritic cells fused to tumor cells based upon there art recognized belief that dendritic cells have superior antigen presenting capabilities.

Applicants therefore respectfully request the withdrawal of the rejection of claims 18-23 under 35 U.S.C. § 103(a).

IV. Conclusion

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 545872000100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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